

We claim:

- 5      ① A method of forming new blood vessels in tissue in a subject which comprises:
- a) isolating autologous bone marrow-mononuclear cells from the subject; and
- b) transplanting locally into the tissue an effective amount of the autologous bone-marrow mononuclear cells, resulting in formation of new blood vessels in the tissue.
- 10      2. <sup>Ab</sup><sub>Al7</sub> The method of claim 1, wherein the tissue is ischemic tissue.
3. The method of claim 2, wherein the ischemic tissue is cardiac muscle tissue.
4. The method of claim 2, wherein the ischemic tissue is skeletal muscle tissue.
- 15      5. <sup>Ab</sup><sub>Al7</sub> The method of claim 1, wherein the tissue is damaged tissue.
6. The method of claim 5, wherein the damaged tissue is heart muscle, skeletal muscle, brain, kidney, liver, an organ of the gastrointestinal tract, a coronary blood vessel, a peripheral blood vessel, an atrophied muscle, skin or lung.
7. The method of claim 5, wherein the damaged tissue is an artificially created site.
- 25      8. The method of claim 1, wherein the subject is a mammal.
9. The method of claim 8, wherein the mammal is a human.
- 30      10. The method of claim 1, wherein the new blood vessels comprise capillaries.

11. The method of claim 1, wherein the new blood vessels comprise collateral vessels.

12. A method of increasing blood flow to tissue in a subject which comprises:

- a) isolating autologous bone-marrow mononuclear cells from the subject; and
- b) transplanting locally into the tissue an effective amount of the autologous bone-marrow mononuclear cells so as to result in formation of new blood vessels in the tissue, thereby increasing the blood flow to the tissue in the subject.

13. The method of claim 12, wherein the new blood vessels comprise capillaries.

14. The method of claim 12, wherein the new blood vessels comprise collateral blood vessels.

15. The method of claim 12, wherein the tissue is ischemic tissue.

16. The method of claim 15, wherein the ischemic tissue is cardiac muscle tissue.

17. The method of claim 15, wherein the ischemic tissue is skeletal muscle tissue.

18. The method of claim 12, wherein the tissue is damaged tissue.

19. The method of claim 18, wherein the damaged tissue is heart muscle, skeletal muscle, brain, kidney, liver, an organ of the gastrointestinal tract, a coronary blood vessel, a peripheral blood vessel, an atrophied muscle, skin or lung.

20. The method of claim 18, wherein the damaged tissue is an artificially created site.

21. The method of claim 12, wherein the subject is a mammal.

22. The method of claim 21, wherein the mammal is a human.

23. A method of treating diseased tissue in a subject which comprises:

- a) isolating autologous bone-marrow mononuclear cells from the subject; and
- b) transplanting locally into the diseased tissue an effective amount of the autologous bone-marrow mononuclear cells so as to result in formation of new blood vessels, thereby treating the diseased tissue in the subject.

24. The method of claim 23, wherein the diseased tissue is ischemic tissue.

25. The method of claim 24, wherein the ischemic tissue is cardiac muscle tissue.

26. The method of claim 24, wherein the ischemic tissue is skeletal muscle tissue.

27. The method of claim 23, wherein the diseased tissue is heart muscle, skeletal muscle, brain, kidney, liver, an organ of the gastrointestinal tract, a coronary blood vessel, a peripheral blood vessel, an atrophied muscle, skin or lung.

28. The method of claim 23, wherein the new blood vessels comprise capillaries.

29. The method of claim 23, wherein the new blood vessels comprise collateral blood vessels.

30. The method of claim 23, wherein the subject is a mammal.

31. The method of claim 30, wherein the mammal is a human.

32. A method of increasing angiogenesis in diseased tissue in a subject which comprises:

- a) isolating autologous bone-marrow mononuclear cells from the subject;  
and  
b) transplanting locally into the diseased tissue an effective amount of the autologous bone-marrow mononuclear cells, thereby increasing angiogenesis in the diseased tissue in the subject.

33. The method of claim 32, wherein the diseased tissue is ischemic tissue.

34. The method of claim 33, wherein the ischemic tissue is cardiac muscle tissue.

35. The method of claim 33, wherein the ischemic tissue is skeletal muscle tissue.

36. The method of claim 32, wherein the diseased tissue is heart muscle, skeletal muscle, brain, kidney, liver, an organ of the gastrointestinal tract, a coronary blood vessel, a peripheral blood vessel, an atrophied muscle, skin or lung.

37. The method of claim 32, wherein the subject is a mammal.

38. The method of claim 37, wherein the mammal is a human.

39. A method of preventing heart failure in a subject which comprises:

- a) isolating autologous bone-marrow mononuclear cells from the subject;  
and  
b) transplanting locally into the heart an effective amount of the autologous bone-marrow mononuclear cells so as to result in formation of new blood vessels, thereby preventing heart failure in the subject.

40. The method of claim 39, wherein the new blood vessels comprise capillaries.

41. The method of claim 39, wherein the new blood vessels comprise collateral blood vessels.

42. The method of claim 39, wherein the subject is a mammal.

43. The method of claim 42, wherein the mammal is a human.

44. A method of regenerating tissue in a subject which comprises:

- a) isolating autologous bone-marrow mononuclear cells from the subject;  
and
- b) transplanting locally into the tissue an effective amount of the autologous bone-marrow mononuclear cells resulting in formation of new blood vessels in the tissue so as to regenerate the tissue in the subject.

45. The method of claim 44, wherein the new blood vessels comprise capillaries.

46. The method of claim 44, wherein the new blood vessels comprise collateral blood vessels.

47. The method of claim 44, wherein the tissue is diseased tissue.

48. The method of claim 47, wherein the diseased tissue is ischemic tissue.

49. The method of claim 48, wherein the ischemic tissue is cardiac muscle tissue.

50. The method of claim 48, wherein the ischemic tissue is skeletal muscle tissue.

51. The method of claim 47, wherein the diseased tissue is a compromised or occluded coronary blood vessel.

52. The method of claim 47, wherein the diseased tissue is a compromised or occluded peripheral blood vessel.

53. The method of claim 47, wherein the diseased tissue is heart muscle, skeletal muscle, brain, kidney, liver, an organ of the gastrointestinal tract, a coronary blood vessel, a peripheral blood vessel, an atrophied muscle, skin or lung.

54. The method of claim 44, wherein the subject is a mammal.

55. The method of claim 54, wherein the mammal is a human.

56. A method of delivering a recombinant nucleic acid molecule to a diseased tissue site in a subject which comprises:

- a) isolating autologous bone-marrow mononuclear cells from the subject;
- b) inserting into the autologous bone-marrow mononuclear cells the recombinant nucleic acid molecule to form transformed bone-marrow mononuclear cells; and
- c) administering to the diseased tissue site an effective amount of the transformed autologous bone marrow mononuclear cells.

57. The method of claim 56, wherein the recombinant nucleic acid molecule encodes a growth factor.

58. The method of claim 57, wherein the growth factor is a cytokine.

59. The method of claim 58, wherein the cytokine is selected from the group consisting of G-CSF, GM-CSF, VEGF, SCF (c-kit ligand), bFGF, a chemokine, and an interleukin.

60. The method of claim 56, wherein the recombinant nucleic acid molecule encodes a cell survival protein.

61. The method of claim 60, wherein the cell survival protein is selected from the group consisting of heme oxygenase, AKT (serine-threonine kinase), HIF $\alpha$  (hypoxia inducible factor), Del-1 (developmental embryonic locus-1), NOS

(nitric oxide synthase), BMP's (bone morphogenic proteins),  $\beta_2$ -adrenergic receptor, and SERCA2a (sarcoplasmic reticulum calcium ATPase).

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62. The method of claim 56, wherein the diseased tissue is ischemic tissue.
63. The method of claim 62, wherein the ischemic tissue is cardiac muscle tissue.
64. The method of claim 62, wherein the ischemic tissue is skeletal muscle tissue.
- 10 65. The method of claim 56, wherein the diseased tissue site is a compromised or occluded coronary blood vessel.
66. The method of claim 56, wherein the diseased tissue site is a compromised or occluded peripheral blood vessel.
- 15 67. The method of claim 56, wherein the diseased tissue is heart muscle, skeletal muscle, brain, kidney, liver, an organ of the gastrointestinal tract, a coronary blood vessel, a peripheral blood vessel, an atrophied muscle, skin or lung. angiogenic site is skeletal muscle tissue.
- 20 68. The method of claim 60, wherein the subject is a mammal.
69. The method of claim 66, wherein the mammal is a human.